

## HUMAN ECOLOGY, DISEASE, AND SCHIZOPHRENIA<sup>1</sup>

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The thesis herein offered is that when inappropriate in kind or amount, the adaptive reactions evoked in an individual in response to threat can result in impairment of organ function and in some instances to tissue damage. Evidence will be cited to show that the functional capacity of the brain also may be restricted following prolonged unsuccessful attempts at adaptation. A further elaboration of the thesis is that the reduction in overall adaptive capacity stemming from this impaired functioning of the brain is relevant to serious disturbance of mood, thought, and behavior, including the clinical syndrome of schizophrenia.

### HUMAN ECOLOGY

These studies have been carried out within the framework of a concept of human ecology that focusses on the interactions between the individual human subject and his environment(1, 2, 3, 4). The attitude of the naturalist is epitomized in the discipline of ecology, dealing as it does with interrelations of organisms and their environment. Those biologists who have taken the broad view of ecology have seen it as embracing the study of any of the pertinent features of the relationship between living organisms and their natural habitat. The ecologist may be properly interested in any aspect of the environment to which the organism must adapt, with the adaptive mechanisms within the organism and the anatomical structures upon which these are based, as well as in the behavior of whole organisms, and that of the colonies and societies which these organisms develop.

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Early in the 20th century the botanist, J. W. Bews(7), suggested that the ecological discipline might be applied profitably to the study of mankind. He saw that those who would deal with problems of human ecology must be prepared to make use of the concepts, knowledge and techniques of many scientific disciplines. To him human ecology is a way of looking at man and of asking questions about him that would be most pertinent to understanding man as a living, constantly adapting organism, never apart from the milieu in which he exists, and constantly interacting with it. Thus, in so far as possible, men would be studied in their natural habitat, behaving as men behave, in the full range of their humanity. This concept has also been evolving independently with us, as a result of our own studies (6, 7, 8, 9, 10, 11, 12, 13).

Such an orientation does not impose the necessity for an intensive investigation of all the factors involved. Indeed, it does not even require the concurrent operation of a "team" of workers with different disciplines, although sometimes necessarily such workers are turned to for specific information. Human ecology is, first of all, the study of man in his setting. Singularly important in this setting are other men, and central to the problem of his health and well-being are his relations to them.

### A THEORY OF DISEASE

Claude Bernard(14), the great French biologist of the mid-19th century, was among the first to see disease as the outcome of attempts at adaptation—attempts which though appropriate in kind, are faulty in amount. Since the defensive response in its intensity can be more destructive than the original assault, an individual may be damaged gravely through the wrong magnitude of his defensive reactions. For instance, the presence of microorganisms in the lung calls forth cellular and humoral reactions that counter invasion, and usually do so effec-



tively. Yet their magnitude when excessive can lead to congestion of the lungs, and to pneumonia. This inappropriate adaptive response becomes especially ominous for the individual when tissue is already involved in a long standing over-reaction, as in chronic lung disease.

Claude Bernard's penetrating definition of disease as resulting from the wrong magnitude of attempts at adaptation, deals mainly with primitive biologic levels of reaction. His observations are also true of man, but disease in humans has a more complex meaning because of man's highly developed nervous system.

The unity of mind and body makes man react adaptively or defensively not only to damaging trauma or microbial forces, but also to threats and symbols of danger. Under circumstances perceived as threatening, he inappropriately may evoke primitive metabolic or reproductive patterns that ordinarily serve to maintain the body and the stock. His adaptive and protective patterns are limited in number, and the form of the reaction depends more on the individual's nature and past experience than upon the particular noxious factor evoking it. Since certain bodily and behavioral patterns are called upon to attain goals that can never be attained through their use, such inappropriate reactions are indefinitely protracted. Functions which are usually phasic become continuous. The tissues involved are pressed beyond their limits. Devices that ordinarily serve to protect the body then destroy tissue.

#### THE THREATENING NATURE OF CHANGING CIRCUMSTANCES

Among the many circumstances perceived as threatening, one of the most threatening is change itself. Rapid and violent social change, by disrupting established relationships, constitutes a serious threat.

Is there evidence that disruptive changes may be relevant to infectious processes? The occurrence of epidemics and increased morbidity from infections among human populations during periods of major change, readjustment and mass dislocation is well known. High mortality from tuberculosis has been associated with increased industrialization during the 19th and 20th centuries

and the resulting migrations from rural to urban life and from one country to another(6, 15). The high mortality has usually been considered the result of exposure to cold and rain, lack of food, excessive effort, crowding, and contact of a migratory population with new and fresh sources of infections to which they had developed insufficient immunity. However, the explanation is probably more complex. For example, in a given society, mortality from tuberculosis has been found to be closely tied to the period in the history of a culture when the use of industrial machines becomes widespread. Mortality reaches its peak about 10 to 20 years after industrialization and thereafter falls off rapidly.

Observations of this kind, led René Dubos(16) the distinguished microbiologist, to conclude :

There is reason to wonder whether any microorganism cannot become the cause of disease if suitable conditions are provided for it. Thus there are many circumstances, some of which are of common occurrence in human medicine, where the physical, chemical, physiological, and probably psychological factors which affect the host, play far more decisive parts in the causation of disease than does the presence of this or that microorganism.

The incidence of hyperthyroidism in Norway increased 100% during the first year of World War II when that country was invaded(21). Other basic endocrine disorders are evident during periods of chaos. Impairment of sexual function with accompanying amenorrhea occurred in nearly all women after interment in the Nazi prison camp of Theresienstadt during World War II and in most of the other camps from which reports are available(18).

#### STUDIES OF ILLNESS INCIDENCE IN LARGE POPULATIONS

A large-scale study of men and women in the context of their environment, and its relationship to their health, has been made in this laboratory(19, 20, 21, 22). The life stories of more than 500 ostensibly healthy people were analyzed and shorter segments of the lives of approximately 3,000 observed. These included not only native American, but also homogeneous groups of

foreign-born persons with an entirely different cultural tradition.

Illness was not spread evenly through these populations. In fact, during the prime of life, about one quarter of the individuals accounted for more than one half the episodes of illness. In some groups there were more than 20 times as many episodes of disabling illness in the "least healthy" members as there were in the "most healthy" members. Some individuals had as little as 20 days of absence from work because of illness in 20 years, and others more than 1,300 days in that length of time.

The persons with the greatest number of illnesses had a wide variety of illnesses. Those who experienced a great deal of illness not only had had many minor, but often numerous major disorders of medical, surgical, and psychiatric nature, including infections, injuries, new growth, and serious disturbances in mood, thought, and behavior.

Episodes of illness often clustered during limited periods of time; that is, there might be many episodes in one or more particular years, contiguous with other periods during which few or no illnesses occurred. These periods of high illness incidence corresponded with the periods perceived by the individual as the most threatening.

Within a given population, when the "most healthy" were compared with those who experienced the greatest amount of illness it was evident that physical hardships, geographic dislocation, exposure to infection, rapid social change, and interpersonal problems occurred with almost equal frequency in their lives. There were, however, differences in the two groups. Those most often ill, in contrast to those least often ill, usually viewed their lives as having been difficult and unsatisfactory. They were more inflexibly oriented toward goals, duties, responsibilities. They reacted sharply to events that confronted them. Typically they were in conflict about pursuing their own ends and ambitions on the one hand, and on the other acting responsibly and according to early learned principles about wives, children, parents and friends. They were "concerned" people, who "took things seriously." Most of them were very much aware of their emotional difficulties and their poor

adjustment in interpersonal relations, and many complained about them. They were anxious, self-absorbed, "turned in," unduly sensitive people who sought much support and encouragement.

In contrast, those who were rarely ill often viewed their lives as having been relatively satisfactory. They came of more stable and complete families, capable of and willing to lend more support. In general they viewed themselves as having had preferred sibling positions, good marriages, and rewarding careers.

It was evident that the relationship between the occurrence of illness and "difficult life situations," is not solely with the difficulty of the situation as seen by a neutral observer but is closely related to the amount of threat in the situation *as perceived by the person who experiences it.*

Diseases in which the relationship between symptomatology and the individual's perception of his environmental setting can be seen especially readily have been termed "psychosomatic." But these studies do not support the view that there is a special category of disease to be designated by this term. With the exception of those instances of grave inborn functional or structural errors that early in life narrowly limit the range of adaptability, either at its simple biological or the more complex neurobiological level, it was seen that symptomatic illnesses of all kinds arise in and are remarkably influenced by environmental circumstances perceived by the individual as threatening.

Disease is the end result of so many interacting factors that the concept of the "cause" of disease in a specific instance becomes almost unmanageable. While it is apparent that inappropriate adaptive responses to threat contribute especially heavily to the initiation of certain syndromes, such as gastrointestinal ulceration or vascular headache for example, the data of these studies also indicate that it is erroneous to establish a separate category of disease in which these inappropriate responses are the primary or sole etiologic factors. Rather, inappropriate adaptive responses mediated through the central nervous system are implicated to some degree in disease of many categories including infectious, degenera-

tive, neoplastic, and psychiatric. Reactions evoked during unsuccessful attempts at adaptation, even when integrated at high levels of brain function and involving widespread physical and chemical processes, are not necessarily accompanied by outward evidence of emotional disturbances or even by the individual's awareness of an altered feeling state. Bodily illness, on the one hand, and disturbance of mood, thought, and behavior, on the other, are thus best seen not as causally related, but as each being a component of the individual's total response to his internal and external environment.

What reference have these points to longevity and to death? There are hints from other sources that years of life can be pressed out of man by catastrophe or prolonged duress. Physicians often see sudden and unexplainable death come to those who are overwhelmed or filled with despair. There is evidence that "bone pointing," "hexing" and excommunication of transgressors of tribal mores may remarkably shorten life if not immediately kill a man(23, 24).

#### ECOLOGICAL IMBALANCE, IMPAIRED ORGAN FUNCTION AND TISSUE DAMAGE IN MAN

Studies from this laboratory have demonstrated that many of the body's organs become more readily damaged during or following periods perceived by the individual as threatening : vasodilatation, edema, dia-pedesis, hemorrhage, erosion, increased friability of tissue, lowered pain threshold and impaired organ function have been observed in the skin(25), nose, airways(26), stomach(27, 28), colon(29), bladder(30, 31), vagina(32), and in the subcutaneous tissues of the scalp(33). These changes could be induced or terminated rapidly by appropriate alteration of the environment, as by interviews which augmented or decreased the perception of threat.

Over the years one organ or system of organs after the other has been studied in persons functioning in the context of their homes and work environment. For example, in a setting which some individuals perceive as presenting a threat of a certain type, the mucous membrane lining of the stomach becomes intensely engorged, its rate of acid secretion greatly accelerated,

and its rhythmic contractions augmented. This is the stomach pattern of a man preparing to eat a meal. Under circumstances that call for entirely different reactions of aggression or striking in anger, the individual has inappropriately evoked an eating pattern. Similarly, the crying-out anger pattern, with hunger—one of the earliest to appear in infancy—may reassert itself in later life during periods of deprivation or repression of longing for emotional support. Since this displacement behavior seen in the eating patterns cannot satisfy such longings, the gastric activity is excessively prolonged and the lining of the stomach may digest itself. Peptic ulceration may ensue(8, 27, 28).

In studies of the large bowel it has been observed that in those who perceive themselves as threatened in a given way, the mucous membranes become engorged and motility and secretion augmented. This is the pattern of ejection, one that could be used in ridding the organism of materials inadvertently taken in, yet it is evoked inappropriately to help the man rid himself of an unattractive interpersonal problem that cannot be dealt with in this way. Abnormal secretions and the by-products of breakdown may then destroy the lining of the bowel, resulting in ulcerative colitis(29).

Observations of the mucous membranes of the nose, upper airways and lungs have shown that circumstances which the individual perceives as threatening may result in engorgement of the mucosae, increase in secretion of mucous, contraction of smooth muscle of the airways, and even spasm of skeletal muscle. Also, the eosinophil and neutrophil cellular content of nasal secretions increases and there is an increase in the number of eosinophils in the circulating blood. The eyes may tear and close. This is the pattern properly evoked by dangerous gases, fumes, dust, and microorganisms and it serves well to shut out, neutralize and wash away. Yet it is also used by some people in dealing with an offensive man-to-man situation. Because of excessive and inappropriate use, the reaction may trigger chronic infection, chronic obstructive disease, and asthma(26). Alterations in the chemical make-up of the secretions within

the lungs may end in tuberculosis by affording an opportunity for organisms to reproduce that otherwise would die.

Under circumstances that threaten an individual's fulfillment of his responsibilities and are met by heightened vigilance, the blood vessels about the head may constrict and the great sheets of muscle of the head and neck go into painful cramp(34-37).

Many skin disorders arise under threatening circumstances because of inappropriate responses of the blood vessels and unusual secretions in the skin(25, 38, 39). Under like conditions, the kidney may be damaged because it gets too little blood, with great outpouring or retention of water and salt(40-45). So also the heart and blood vessels of the body may overwork and contract excessively as though the individual were stopping a mortal hemorrhage, or facing a crisis of fight or flight—when, as a matter of fact, he may be sitting inertly in a chair(46, 47).

When a person feels his prestige endangered, the glands of internal secretion—the pituitary, the thyroid, and the adrenals—may respond as though his very existence were in jeopardy, as by starvation, or by the sudden unusual demands of very low temperature or violent action(48, 49).

Contraction of the muscles of the extremities and back, inappropriately responding to threatening circumstances by preparing the individual for prompt action that never takes place, can cause severe cramps and aches(50).

No organ or part of the body is spared in these inappropriate responses that are so suggestive of the displacement behavior patterns of rats(51) and gulls(52) and fish(53) studied by the animal behaviorists. Yet not all reactions that end as disease in man can be seen as "displacement" patterns. Migraine headache which results from the painful dilatation of the blood vessels of the head coupled with a local sterile inflammatory reaction often occurs not during stressful periods but after their termination(34, 54).

Distention of cranial arteries is a significant factor in vascular headache of the migraine type. Also, it is evident that the accumulation of a pain threshold lowering substance in the walls of these arteries as

well as in the adjacent perivascular, areolar and supporting tissues, is an essential feature of the headache attack. Accordingly, attempts were made(55) to define the properties of perfusate collected during migraine attacks from subsurface tissues in the region of the temporal and frontal vessels of the head. The specimens collected from the head during headache attacks predictably contained a substance that could be distinguished from serotonin, ATP, substance P, acetylcholine, and histamine although these and other substances could also be present. This agent relaxed isolated rat duodenum, contracted rat uterus and depressed the blood pressure of the rat. The substance has many of the properties of bradykinin, but when analyzed quantitatively using several assay procedures it was evident that it is not identical with bradykinin, but closely resembles the vasodilator polypeptide "neurokinin" that has been found in this laboratory(56) to be present in perfusate collected during the onset of axon reflex "flare" in the skin. The amount of active agent found in the specimens paralleled the intensity of the headache attack. The increased content of polypeptide found locally and the relevant protease could account for many of the features of vascular headache of the migraine type: the polypeptide is an extremely powerful vasodilator, it induces pain and lowers pain threshold when reinjected intradermally, and it increases capillary permeability. Vascular headache of the migraine type thus can be seen as the consequence of an excessive accumulation of a neurogenic agent implicated in local vasomotor control, resulting in a local sterile inflammatory reaction.

#### THE NERVOUS SYSTEM AND PRIMITIVE BIOLOGICAL REACTIONS

A recent series of investigations(38, 52, 58, 59) has focussed on ways in which activity of the nervous system can influence inflammatory reactions and vulnerability to injury. It was demonstrated that peripheral nerve action can result in alterations that both damage the tissue subserved and alter the reaction to injury. Thus, significantly more skin damage occurred in the "flare zone" of an axon reflex than in adjacent

control areas in response to similar amounts of noxious stimulation. Also, immersion of the lower extremities in water at 43° C. resulted in widespread vasodilatation and a transient lowering of the pain threshold and heightened tissue vulnerability as measured on the hand and thorax.

Following standard amounts of noxious stimulation on the forearm during hypnosis, increased inflammatory reaction and tissue damage was observed in subjects to whom repeated and forceful suggestions had been made that the forearm was tender, painful and injured. Diminished tissue damage was observed when the subject was told his forearm was "anesthetic." Recordings of finger pulse amplitude and skin temperature indicated that local vasodilatation following exposure to noxious stimulation is larger in magnitude and persists longer in the "vulnerable" arm; whereas these reactions are minimized in the arm perceived by the individual to be anesthetic.

The subcutaneous tissue of the forearm was perfused with normal saline and the perfusate analyzed before and after an axon reflex flare was induced by faradic stimulation of the skin (or by intradermal injection of histamine) adjacent to the perfused region(56, 58, 60, 61). With the onset of the axon reflex flare, a substance predictably occurred in the perfusate that relaxed isolated rat duodenum, contracted rat uterus and depressed the arterial blood pressure of the rat. A constant ratio of activity on the several test models indicated that the observed effects of the specimens are due to a single substance. The substance did not occur in perfusates collected during non-neurogenic vasodilatation following ischemia of the arm (reactive hyperemia). The name "neurokinin" has been suggested for the substance thus formed during augmented activity of neurons. A polypeptide with the same properties as the agent observed during axon reflex flare as well as an enzyme capable of forming it when incubated with plasma globulin also have been found in the cerebrospinal fluid of some patients with disorders of the central nervous system. Neurokinin and the relevant protease have also been found in perfusate of the cerebral ventricles of laboratory animals during stimulation of the

brain(70) and in perfusates of peripheral nerve during stimulation(71). In addition to its role in the axon reflex of the skin, neurokinin may serve in local vasomotor control within the central nervous system and may possibly have more direct effects on neuronal function.

Enhanced inflammation has been shown to be effective in combatting invasion by microorganisms and in the rapid elimination of tissue breakdown products of injury. The view is proposed that man includes among his adaptive and protective devices, neural reactions integrated at the highest levels that heighten inflammation in the peripheral tissues and increase the local susceptibility and reaction to injury—thus enhancing the protection of the whole organism at the cost of the integrity of a part. Such reactions at times may be essential to survival. But, if evoked inappropriately or excessively, they can contribute to disease since non-noxious stimulation becomes noxious and mildly damaging stimuli result in greater injury.

In brief, neural activity involving the segmental, brain stem, and cortical levels can modify reaction to noxious stimulation in the peripheral tissues so as to augment or suppress inflammation and tissue damage. A change in attitude towards noxious stimulation may thus increase or decrease inflammatory reactions and tissue damage in part through local alterations in vaso-motor function with concomitant increase or decrease of proteolytic enzymes, polypeptides and other humoral substances in the tissue fluid.

#### THE NATURE OF THE HIGHEST INTEGRATIVE FUNCTIONS OF MAN

Through studies of those with loss of tissue from the cerebral hemispheres it was found that the defects characteristic of conventional concepts of "dementia" or "organic brain damage" (defects in memory, judgment, orientation, simple perception etc.) were not predictably present unless the loss was relatively large (more than approximately 120 grams). Indeed, the mean verbal intelligence quotient of those subjects with up to 120 grams tissue loss was not different from that of the general intact population. However, even those

with as little as 30 gram tissue loss predictably demonstrated defects in other aspects of their adaptive capacity. Thus it was found necessary to expand the concept of the functions of the cerebral hemispheres.

Several categories of highest level functions have been defined. First are those functions having to do with the expression of needs, appetites, and drives. Fall-off in these functions is manifest in decreased seeking of challenge and adventure, restriction of imagination, lessened human association and exchange, diminished aspiration and striving, abandonment of previously cherished goals, passive acceptance of circumstances, lessened sexual activity, and when the damage is severe, inadequate response to even the minimal requirements of food, shelter, and warmth.

Second, are those functions having to do with the capacity to respond to symbols as substitutes for biologically significant events, thus employing effectively the mechanisms for goal achievement. These enable the individual to anticipate dangerous or propitious circumstances and to learn, perceive, know, remember, arrange, plan, invent, explore, postpone, modulate and discriminate. Important in this category is the capacity to eliminate responses when they are no longer appropriate.

Third, are those functions that enable man, under circumstances of duress, to integrate elaborate behavior patterns of a defensive or protective nature that are appropriate, adequate, socially acceptable, and sustained.

Fourth, are those functions having to do with the maintenance of organization. These, as mentioned above, serve to lend continuity and maintain stability and proper speed of response and are especially important during periods of stress.

The components of the highest integrative functions are not equally fragile. Impairment of speed of response, spontaneity, imagery, creativity, rapid learning, ease of abandoning a pattern when no longer appropriate, capacity for abstraction, and ability to resist the disorganizing effects of stress are evident in subjects with loss of even small amounts of tissue, whereas vocabulary, long utilized skills, behavior patterns, and premorbidly acquired informa-

tion are not significantly impaired until there is a much greater loss of tissue. With major loss of tissue from the cerebral hemispheres, there is progressive inactivity and finally coma and death.

#### THE HUMAN BRAIN AND ENVIRONMENTAL INTERACTION

There is much to indicate that the brain itself, in integrating highest level adaptive responses, may be damaged as a consequence of improper interaction between organism and environment.

In men, and in some laboratory animals, the development of brain function may be retarded when in infancy they are deprived of suitable challenge, adequate stimulation, the protection of a parent, and opportunities for successful interaction with the environment. There are instances of infants and children raised in relentlessly hostile environments or in those permitting of no continuing human relationship who have not matured(64). Also, aged persons deteriorate rapidly when they are deprived of their work and social responsibilities.

In man total isolation and severely restricted sensory stimulation are followed by temporary impairment of high level brain functions. Men subjected to the prolonged abuse and hatred of their fellows, as in prison, behave as though their heretofore actively functioning brains were severely damaged. They pass through predictable states of progressive impairment, comparable to the impairment observed in subjects with progressive loss of brain substance. Even when sleep and food are adequate, complete isolation, lack of opportunity to talk, repeated failure, frustration, and reviling by other men can cloud the mind and may make a man confabulate, become more suggestible, and cause him to rationalize behavior previously unacceptable(65).

The quantitative methods developed through the study of individuals with cerebral ablations permitted assessment of highest level brain function in ostensibly intact individuals who had experienced prolonged periods of unresolved difficulties in adaptation. It was found that persons with no evidence of gross anatomic disease of the brain but who, for long periods had achieved no effective adaptation and had

experienced longstanding anxiety and other disturbances in behavior and mood (both with and without bodily disorders), exhibited severe thinking and adaptive difficulties. Indeed, they performed in their usual lives and laboratory test procedures as though moderate and sometimes massive amounts of brain had been damaged or removed. Those with effective defenses such as blaming, rationalizing, sublimation, denying, pretending, or withdrawing from participation, showed less deterioration in brain function. But when these defenses were no longer adequate or stress had been too prolonged, these individuals too, demonstrated a persisting impairment of highest level brain functions.

The observed "mass action" relationship between the highest level functions and the aggregates of neurons in the cerebral hemispheres may give a clue to the nature of the process. For highest level functions the number and degree of arrangement of nerve cells is of central importance, and the pattern of specific localized connections, so important for lower level functions, is of lesser significance. Order itself becomes the relevant attribute for understanding of the relationship between the neuron and the highest level functions.

The property of being highly ordered, is of course, not limited to the brain, but is shared by all living cells. However, the density of arrangement within different bodily tissue varies greatly, reaching its apex in the brain. Thus in our view, although all tissues contribute, by virtue of this high density of arrangement and their great mass, the cerebral hemispheres of man contribute more to highest level functions than do other structures. In a sense, then, "mind" may be said to reside in all cells of the body, a view in keeping with the intuition of the ancients who were reluctant to name the brain or any single organ as the sole residence of mind(69).

The concept that the organization of highly ordered systems featured by purposive, self-regulatory, goal-oriented activities is in keeping with the contemporary orientation of biologists. Sinnott(70) defines mind as "whatever directs the development of an organism toward goals set up

within its living stuff." Accordingly the relationship of the brain to the mind is viewed by us as follows: Mind is the aggregate of purpose and needs, arising from the parts and the whole of the human organism, whereas the brain in addition to contributing to purpose, is the organ of means for maximum adaptive versatility to achieve these ends.

#### ADAPTIVE REACTIONS AND PSYCHOSIS

These considerations of the consequences of unresolved difficulties in adaptation long maintained, encourage an attempt to reassess the place of psychoses within a general theory of disease. The orientation for this effort is derived from the observation that many hospitalized patients with chronic schizophrenia exhibit a serious impairment of functions of the cerebral hemispheres, an impairment with all of the features found predictably in those with major tissue loss from the isocortex of the cerebral hemispheres, but colored and overlaid with special features that make possible the ready differentiation of schizophrenia in most instances(67, 71, 72).

The nature of the process of schizophrenic deterioration is ill-defined, and indeed, it remains uncertain whether schizophrenia is a single disease entity, even though psychoses of the schizophrenic type occur more commonly in some family stocks.

The evidence previously cited indicates that when an individual perceives himself to be dangerously or overwhelmingly threatened for long periods, and some satisfactory level of overall adaptation cannot be achieved, the functions of the brain are impaired (at first readily reversibly and ultimately less so). Schizophrenic psychoses may be initiated in individuals during such periods. But, in this regard, the schizophrenic reaction differs in no essential way from many other human symptom complexes, and in fact in itself allows of no inferences as to the pathological process involved. As indicated previously, infections, metabolic disorders and behavior changes as well as various enzymatic disturbances may all be initiated in such untoward circumstances.

In addition to the demonstration of serious deterioration of the highest integrative

functions in moderately advanced schizophrenic patients, it has been shown that the cerebrospinal fluid of many schizophrenic patients (73-75) contains unusual amounts of a proteolytic enzyme, unusual proteins, occasionally polypeptides and other products of proteolysis. These substances are also found in the spinal fluid of patients with inflammatory and progressive degenerative diseases of the central nervous system and even after periods of augmented central nervous system activity in otherwise intact persons and laboratory animals (62). The occurrence of increased amounts of these non-specific accompaniments of catabolism in those with schizophrenic reactions suggests that a significant (yet perhaps reversible) alteration in metabolism occurs in the brains of patients so classified. Moreover, the accumulated proteolytic enzyme, other agents, and polypeptides in themselves could contribute to impairment of the functions of the brain.

The data about the abnormality in the spinal fluid bespeak only altered function without defining a category of disease. However, the described change in enzymatic content is compatible with the suggestion that in these patients there is a metabolic disturbance within the central nervous system, either primary or secondary.

A working hypothesis for the mechanism of the impairment in the functions of the cerebral hemispheres of patients with schizophrenia may be suggested. Neuronal excitation and alterations in the patterns of neuronal activity during faulty adaptation, if sustained could lead to persisting disorganization of neural patterns. Since for effective integration the highest level brain functions are dependent upon uninterrupted and proper interaction with the environment and suffer rapidly when this exchange is restricted or distorted, prolonged disorganization of neural patterns would further interfere with proper interaction and perpetuate a cycle that could lead to long-lasting impairment. Secondly, the defensive reactions (denying, blaming, shutting out, etc.) result in a reduction of proper interaction of the individual with his environment since they limit, distort, or block perception of the environment or

reduce the participation of the individual.

Further, excessive or prolonged neural activity under such adverse conditions may result in the elaboration of substances originating outside or inside of the brain that interfere with neuronal function. An inborn metabolic defect could contribute to this dysfunction.

#### DISCUSSION

Since man is a tribal creature with a long developmental period, he depends for his very existence on the aid, support and encouragement of those about him. He lives so much in contact with others and he is so deeply concerned about their expectations of him, that perhaps his greatest threat is their disapproval or rejection. Events having to do with his place in his society take on a major significance and man often functions best when his own ends are totally subordinate to the common end. Inversely, when he is frustrated in such efforts, or rejected by his group, the individual may evoke destructive inappropriate adaptive and defensive reactions or even die. Man is jeopardized not only by those forces that threaten survival of self and kin and opportunities for procreation, but he is also endangered when through the actions of others, his growth, development, and fulfilment of individual proclivities are blocked, and even when his esthetic needs and creative potential are not satisfied.

Challenge is essential and some threat is desirable, if not necessary, for proper human development. But threats to the stability of intimate human relations, especially during the dependent years, and those that wipe out hope and faith in men can have grave effects.

Many persons have a proclivity for reacting to threat with one particular adaptive pattern, for example, one involving the stomach, rather than the large bowel; or with blaming rather than compulsive activity. They may react to threats in this way for many years, using other patterns only now and then: once established many patterns appear to be self-perpetuating. Several members of one family often show similar patterns. However, even though a given person when confronted by a similar situation usually reacts in the same way, when a new significance is attached to the

situation, new adaptive patterns may appear. In the course of a lifetime several different patterns may be established in those who are threatened by numerous circumstances or who only transiently achieve a suitable adaptation.

Man's special capacity to react to *symbols* as though to significant *events*, enhances his ability to perceive threats as well as to increase his satisfactions. How, then, he perceives his immediate environment depends on his inborn equipment and early conditioning as well as on a host of life experiences. Since pain or damage to tissue provokes vigorous general and local protective reactions, symbols of destructive experience can also evoke such reactions, often to a degree far more costly to the individual than the actual effects of the assaults they symbolize. Moreover, aspiration, creativity, abhorrence of boredom and need of change are central aspects of human activity. At times of his greatest vigor, man is ready to abandon the safe, the certain, the predictable and the secure for challenge, increased responsibility, uncertainty, adventure and exploration. The utopias, the idyllic pastoral tranquility he dreams and talks about, he forgoes to fulfil his humanity. In so doing he may seriously jeopardize the adaptative arrangement most compatible with health. Illnesses of all kinds—impairment in function, reversible or otherwise, with and without obvious tissue damage—are aspects of attempts at adaptation during striving to attain human goals.

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